Responsiveness of raised pulmonary vascular resistance to oxygen assessed by pulsed Doppler echocardiography

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Abstract

***Objective*—To assess whether changes in Doppler echocardiographic indices in the pulmonary artery correlated with changes in pulmonary vascular resistance.**

***Design*—Acceleration time, ejection time, maximal flow velocity, and velocity time integrals were measured at the same time as pressure and oxygen saturation measurements in room air and during 10 minutes of oxygen breathing in the catheterisation laboratory. Pulmonary vascular resistance and pulmonary blood flow (Qp) were calculated from catheterisation data by use of the Fick principle.**

***Patients*—14 consecutive patients with a congenital heart defect and a left to right shunt associated with raised pulmonary artery pressure who underwent routine diagnostic cardiac catheterisation to assess their pulmonary vascular resistance.**

***Results*—Though pulmonary vascular resistance and systolic pulmonary artery pressure fell significantly during oxygen administration, there was no significant change in the acceleration time or ejection time. Peak velocity increased significantly during oxygen administration. During oxygen breathing Doppler derived measurements of pulmonary flow showed a significant increase in Qp similar to the increase in Qp measured by the Fick principle. There was no significant correlation between the fall in pulmonary vascular resistance and the increase in acceleration time or ejection time, increase in peak velocity, increase in pulmonary artery diameter, or increase in Doppler derived pulmonary blood flow.**

***Conclusions*—Measurements of acceleration and ejection time by Doppler echocardiography did not predict the response of pulmonary artery pressure and resistance to oxygen. Though changes in maximal flow velocity across the pulmonary artery and in Doppler derived pulmonary blood flow measurements became significant during oxygen breathing, the correlation of these changes with fall in pulmonary vascular resistance was poor.**

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Accepted for publication 14 May 1991

A prolonged increase in pulmonary artery flow and pressure can lead to the development of irreversible pulmonary vascular disease especially in children with large interventricular communications.[1] To judge soperability the standard technique is to measure pulmonary artery pressure and calculate pulmonary vascular resistance by the Fick method in the catheterisation laboratory.[1 2] Recently several studies have indicated that analysis of the pulmonary artery flow velocity profile by Doppler echocardiography may be a valuable non-invasive means of evaluating pulmonary artery pressure.[3–5] We evaluated the usefulness of Doppler echocardiography in assessing changes in pulmonary artery pressure and resistance after oxygen administration by comparing Doppler derived indices with simultaneous measurement of pulmonary artery pressure and calculation of pulmonary vascular resistance by the Fick principle during cardiac catheterisation.

Patients and methods

STUDY GROUP AND PATIENT SELECTION

We studied 14 children. All had raised pulmonary artery pressure as part of their congenital heart defect. Table 1 lists the diagnoses. Six children (patients 3, 5, 6, 7, 10 and 13) had Down's syndrome. Because sedated patients, especially those with Down's syndrome, can have altered pulmonary vascular resistance because of hypercapnia or acidosis,[2] we included only patients with a P_{CO_2} of <50 and a pH of $>7{\cdot}34$. Because pulmonary vascular resistance varies spontaneously by up to 36% from day to day,[6] we only analysed data from patients whose change in pulmonary vascular resistance exceeded 40%.

Table 1 Clinical data on 14 patients with pulmonary artery hypertension

Patient	*Diagnosis*	*Age at time of study (yr)*
1	VSD, coarctation of the aorta	3·3
2	AVSD	0·5
3	AVSD	8·4
4	VSD	0·4
5	VSD	1·5
6	AVSD	0·5
7	AVSD	0·5
8	Mitral stenosis, subaortic stenosis, coarctation of the aorta	0·8
9	VSD	0·9
10	AVSD	1·1
11	VSD	0·2
12	VSD, coarctation of the aorta	0·6
13	AVSD	0·2
14	VSD, PDA	0·9

AVSD, atrioventricular septal defect; PDA, patent ductus arteriosus; VSD, ventricular septal defect.

ECHOCARDIOGRAPHIC METHODS

Commercially available equipment consisting of a Ultramark 8 or 9 imaging system by Advanced Technology Laboratories was used for the echocardiograms, which were obtained with either a 5 or 7·5 MHz transducer. The images were recorded on 1/2 inch videocasette tape. The echocardiographic study was performed in the cardiac catheterisation laboratory simultaneously while the patient was breathing room air and for 10 minutes while the patient was breathing 100% oxygen through a face mask. The Doppler flow in the pulmonary artery was analysed from the parasternal short axis view approximately 1 cm distal to the pulmonary valve. We used an off-line computer (Kontron 200) to evaluate five consecutive cardiac cycles. The Doppler flow curve across the pulmonary artery was manually traced on the electronic drawing board with a light pen. The following variables were measured: peak velocity in the pulmonary artery (m/s); right ventricular ejection time (ET), from the onset of ejection to zero flow (ms); and acceleration time (AT), as the time interval from the onset of ejection to peak flow velocity (ms). Because AT and ET may be affected by changes in heart rate,[7 8] we also calculated the ratio AT/ET and the corrected AT obtained by dividing AT by the square root of the RR interval from the measurements mentioned above. The pulmonary systolic velocity time integral (VTI) was determined by digitising and integrating the area under the Doppler velocity curve according to the following equation: $VTI = \int ET \times pkV(t)\,dt$, where ET is the ejection time and pkV the instantaneous peak velocity. Pulmonary blood flow was calculated by multiplying the VTI by the luminal area of the pulmonary artery measured at the pulmonary valve level.[9]

CARDIAC CATHETERISATION

All children underwent cardiac catheterisation. Sedation consisted of morphine 0·1 mg/kg in combination with flunitrazepam 0·04 mg/kg given intramuscularily. Pressures were measured with standard fluid filled catheters coupled to a Statham transducer. We measured pulmonary and systemic blood flows by the Fick method using measured oxygen consumption and oxygen content derived from radiometer oxygen saturation. Mixed venous oxygen saturation was obtained from the superior and inferior venae cavae (SVC and IVC) and calculated as (3 × SVC) + (1 × IVC) saturation divided by four.[2] Pulmonary venous blood was obtained from the left atrium in eight patients and from a pulmonary vein in six. All pressure recordings and oxygen saturation samplings were performed before and at the end of a 10 minute period of breathing 100% oxygen by face mask. A Doppler echocardiographic study was performed at the same time. Pulmonary and systemic resistances were derived from the pressures and flows across the respective vascular beds. The ratio between pulmonary and systemic vascular resistance was also calculated and it was regarded as an important indicator of the responsiveness of the pulmonary vascular bed because errors in oxygen capacity cancel out[10] and use of the ratio avoids the need to index for flows and resistances.[2]

STATISTICAL ANALYSIS

Data are expressed as mean (SD). Linear regression analysis was used to determine the correlation between changes in pulmonary vascular resistance and Doppler derived variables. We used Student's paired t test to compare data. A p value of $<0·05$ was regarded as significant.

Results

Table 2 shows the results of the measurements before and during oxygen breathing of the pulmonary artery Doppler flow curve and pulmonary artery pressure during the cardiac catheterisation. Table 3 shows the changes in the pulmonary artery flow profile and measurements obtained at cardiac catheterisation during oxygen administration. The pulmonary vascular resistance and ratio of pulmonary vascular to systemic vascular resistance changed significantly, whereas there was no significant change in the acceleration or ejection time. Table 4 shows the changes in pulmonary artery luminal area and pulmonary blood flow determined either by Doppler echocardiography or by Fick principle during oxygen breathing.

Linear regression analysis showed no

Table 2 Cardiac catheterisation and Doppler echocardiographic data in 14 patients with pulmonary artery hypertension

	PA pressure (mm Hg)		*PA resistance (U.m²)*		*Acceleration time (ms)*		*Acceleration time/RR*		*Ejection time (ms)*		*Acceleration/ ejection time*		*PA Doppler velocity (m/s)*	
Patient	*Room air*	O_2	*Room air*	O_2	*Room air*	O_2	*Room air*	O_2	*Room air*	O_2	*Room air*	O_2	*Room air*	O_2
1	103	100	17·2	10·1	48	63	1·9	2·7	138	154	0·35	0·41	0·48	0·64
2	78	55	2·9	0·3	75	97	3·7	4·9	203	193	0·37	0·5	1·61	1·52
3	65	48	9·4	1·1	99	115	3·8	4·0	225	246	0·44	0·46	0·96	0·71
4	70	67	3·5	1·5	116	94	6·0	5·2	214	231	0·54	0·4	1·41	1·66
5	78	55	2·1	0·1	65	102	3·4	4·7	113	263	0·57	0·39	0·78	1·11
6	75	81	4·1	3·3	53	97	2·7	4·3	177	222	0·30	0·42	0·75	1·27
7	72	72	3·0	0·6	100	111	4·8	5·4	234	266	0·43	0·42	1·26	1·64
8	108	88	18·0	11·5	94	89	5·7	4·0	207	224	0·45	0·40	0·65	0·74
9	76	74	14·5	6·0	74	109	3·2	4·7	193	194	0·56	0·56	0·63	0·85
10	73	71	2·7	0·9	69	101	3·5	4·3	211	236	0·33	0·43	1·23	1·22
11	74	65	7·1	1·1	107	111	5·4	5·4	212	214	0·50	0·52	1·40	1·71
12	75	69	10·8	5·1	66	110	2·9	5·5	140	178	0·47	0·62	0·71	1·08
13	74	56	5·1	0·9	112	113	5·9	5·9	220	200	0·56	0·57	1·53	1·80
14	78	65	6·2	2·1	130	82	6·2	4·2	242	220	0·54	0·37	1·29	1·42

PA, pulmonary artery.

Table 3 Doppler flow curve and cardiac catheterisation data before and during oxygen breathing in 14 patients with pulmonary artery hypertension

Variable	*Before*	*During*	*p Value*
AT (ms)	83·9 (26)	94·9 (28)	NS
Heart rate (beats/min)	136·6 (21)	131·6 (31)	NS
Corrected AT (ms)	3·9 (1·3)	4·3 (1)	NS
ET (ms)	184·2 (38)	203·8 (47)	NS
AT/ET	0·44 (0·08)	0·43 (0·08)	NS
Flow velocity (m/s)	0·97 (0·38)	1·08 (0·4)	0·05
PA pressure (mm Hg)	83·6 (17·9)	74·3 (18·6)	0·007
Qp/Qs	1·5 (1·1)	7·1 (6·8)	0·04
Rp (U.m^2)	13·1 (12)	5·5 (5·1)	0·006
Ratio Rp/Rs	0·79 (0·75)	0·29 (0·31)	0·01

Pa, pulmonary artery; AT, acceleration time; ET, ejection time; Rs, systemic vascular resistance; Rp, pulmonary vascular resistance.

Table 4 Pulmonary artery diameter, VTI, and Qp determined before and during oxygen breathing by Doppler or Fick principle in 14 patients with pulmonary artery hypertension

	PA luminal area		*VTI*		*Qp by Doppler*		*Qp by Fick*	
Patient	*Before*	*During*	*Before*	*During*	*Before*	*During*	*Before*	*During*
1	2·7	4·0	4·6	10·3	2·1	2·5	4·0	6·4
2	1·6	1·8	16·1	20	4·0	4·4	3·0	6·6
3	3·0	3·3	12	16·9	3·8	3·9	3·0	5·4
4	1·6	1·7	16·3	21·2	3·9	6·6	2·4	5·1
5	0·7	0·9	5·7	15·5	0·7	1·8	2·6	22·0
6	0·8	0·9	18·8	30	2·2	4·4	3·4	8·1
7	1·4	1·5	16·4	20·3	3·0	4·1	2·7	4·8
8	1·6	1·9	6·3	8·7	1·5	2·0	2·6	3·1
9	1·8	2·1	5	6·7	1·1	1·3	3·1	6·7
10	1·4	1·7	11·4	19·4	2·7	4·2	2·1	4·3
11	0·9	1·6	16·7	22·5	2·1	5·4	2·6	5·7
12	1·9	2·4	6·3	10·4	1·7	2·9	1·4	2·5
13	0·2	0·5	18·3	24	1·9	2·0	1·8	4·6
14	0·8	0·8	17·5	17·5	1·9	2·1	1·8	2·2
p	$p < 0·003$		$p < 0·001$		$p < 0·002$		$p < 0·01$	

PA, pulmonary artery; VTI, velocity time integrals; Qp, pulmonary blood flow.

correlation between the fall in pulmonary vascular resistance during oxygen breathing and the increase in AT ($r = 0·22$; $p < 0·45$) or the AT corrected for heart rate ($r = 0·05$; $p < 0·84$), ET ($r = 0·42$; $p < 0·14$), AT/ET ($r = 0·1$; $p < 0·73$), increase of peak flow velocity across the pulmonary valve ($r = 0·2$; $p < 0·49$), increase in pulmonary artery luminal area ($r = 0·52$; $p < 0·06$), increase in velocity time intervals ($r = 0·55$; $p < 0·04$), or increase in pulmonary blood flow ($r = 0·42$; $p < 0·16$).

Discussion

Doppler echocardiography is safe, relatively easy to perform, and repeatable. It could be useful in clinical studies of congenital heart defects that increase pulmonary artery flow and pressure, because patients could be followed serially and their response, in terms of pulmonary vascular resistance, to oxygen or pulmonary vasodilator drugs estimated.

Initial reports about the specificity and sensitivity of measurements of acceleration and ejection time in distinguishing patients with abnormally high pulmonary artery pressure from those with normal pulmonary artery pressure were promising.[3-5] The results of some of these studies have recently been questioned. Drawbacks include the variability in Doppler flow curves attributable to differences in the pulmonary artery sampling site,[11] the inability of the method to detect moderate increases in pulmonary artery pressure,[12] and its inability to detect significant changes in pulmonary vascular resistance in response to pulmonary vasodilator treatment.[13]

Panidis *et al* reported considerable differences in acceleration time, ejection time, and maximal flow velocity across the pulmonary valve in controls with normal pulmonary artery pressure and in patients with increased pulmonary artery pressure when four different sampling sites were used: right ventricular outflow tract, pulmonary valve, centre of main pulmonary artery, and near the main pulmonary artery wall.[11]

In an animal study Gutgesell *et al* showed that the Doppler velocity flow indices were relatively insensitive to moderate increases in pulmonary artery blood flow or pressure.[12] In a clinical study in patients with primary pulmonary hypertension no significant difference in acceleration or right ventricular ejection time could be detected between a normal control group and patients in whom raised pulmonary artery pressure had been measured at a previous cardiac catheterisation.[13]

In a study of 21 children with ventricular septal defect 11 responded significantly to vasodilator drugs during cardiac catheterisation. There was no significant difference in terms of acceleration or right ventricular ejection time between responders and non-responders.[13] In another study of six infants no difference was detected in the Doppler flow indices before and after oxygen breathing.[14]

Slight but significant changes in maximal pulmonary artery flow velocity in patients with pulmonary hypertension responsive to pulmonary vasodilator treatment have been reported.[13 15] One group noted that three patients with pulmonary obstructive disease and a poor

response to vasodilator treatment had a flow velocity of < 1 m/s and speculated that irreversible pulmonary hypertension can be assumed in a patient whose peak velocity remains < 1 m/s after pulmonary vasodilation.[15] However, our data and the study from Cooper *et al*[13] do not support this assumption. Cooper *et al* found one patient with a peak pulmonary artery velocity of 1·24 m/s after vasodilator treatment whose lung biopsy specimen showed grade IV pulmonary vascular disease.[13] We successfully operated on a child (patient 9 in tables 1 and 2) whose velocity after oxygen administration was 0·85 m/s and whose pulmonary vascular resistance fell to 6 units × m^2, yielding a Rp/Rs ratio of 0·3 after oxygen breathing.

In all our patients pulmonary artery blood flow assessed by Doppler echocardiography increased significantly. This was in part due to an increase in the pulmonary artery luminal area. Again we could not show any positive correlation between an increase in Doppler flow across the pulmonary artery or an increase in pulmonary artery luminal area and the decrease of pulmonary vascular resistance.

The finding that Doppler flow velocity or velocity time integrals in the pulmonary artery are not reliable indicators of the reversibility of increased pulmonary vascular resistance is not surprising because the Doppler flow velocity curve is influenced by the sampling site in a similar way as the Doppler time indices.[16 17]

The clinical application of the pulsed Doppler method of assessing pulmonary resistance is further limited by the fact that the spontaneous variability in pulmonary blood flow is presumably increased in patients with primary pulmonary hypertension.[18] In this group spontaneous changes in pulmonary artery pressure of 22% and pulmonary vascular resistance of 36% have been reported.[6] Because of this high variability in pulmonary vascular resistance we excluded from our study those patients whose pulmonary vascular resistance fell less than 40% during oxygen administration. The high spontaneous variability of pulmonary vascular resistance also limits the applicability of cardiac catheterisation studies for the assessment of the responsiveness of pulmonary vascular resistance to oxygen.[15 19]

Published reports[12–14] and our data show that cardiac catheterisation remains the best method of assessing the potential reversibility of increased pulmonary vascular resistance.

This work was presented in part at the XXVI annual meeting of the Association of European Pediatric Cardiologists in Oslo, June 12–15th 1990.

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